

### **REMARKS**

Claims 68-97 are pending.

No new matter has been added by way of the present submission. For instance, claim 82 has been placed into independent format by including the subject matter of claims 68 and 72. The incorporated language of claim 68 has also been modified to define the “analog” and “derivative” as supported by the present specification at, for instance, pages 19-22. Such locations also provide support for newly added claims 85-88 and 91-94. The language concerning “prevention” has also been changed to “inhibition” as supported by the present specification at page 3, line 25. Newly added claims 89, 90, 95, 96 and 97 are supported by pending claims 82 and 84 as well as the specification as filed. Thus, no new matter has been added.

In view of the following remarks, the Examiner is respectfully requested to withdraw all rejections and allow the currently pending claims.

### **Election/Restrictions**

The Examiner has acknowledged Applicants election with traverse of Group II, claims 82 and 83 in the reply filed on October 24, 2008 and that the traversal is not found persuasive for the reasons set forth on pages 2-3 of the outstanding Office Action.

In this regard, Applicants respectfully submit that claim 84 presents a method of binding to *H. pylori* with a saccharide substance according to the invention. Applicants’ opinion is that this embodiment belongs to invention group II, because this method may be included for therapeutic inhibition of *H. pylori* and may thus be an integral part of this therapy.

The method of claim 84 is dependent on a novel substance which is the complex of *H. pylori* with the oligosaccharide substance. The Examiner refers to Jacquinet et al. as indicating the existence of this oligosaccharide substance. However, as stated by the Examiner, Jacquinet is silent about the binding of the substance to *H. pylori* and therefore also about the novel complex substance related to the subject matter of the claim, i.e., the physical complex of the oligosaccharide sequence and *H. pylori*. It should be realized that this complex is not disclosed in Jacquinet as such and thus it cannot be an inherent property of the disclosed oligosaccharide alone.

For at least this reason, Applicants request examination of claim 84 as well as claims dependent thereon.

### **Claim Objections**

Claim 82 is objected to for the reasons set forth on page 4 of the outstanding Office Action. Applicants respectfully traverse this objection in view of the amendment to the claim. Thus, it is respectfully requested that this objection be withdrawn.

### **Issues under 35 U.S.C. § 112, first paragraph**

Claims 82 and 83 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth on pages 4-11 of the outstanding Office Action.

Applicants respectfully traverse this rejection.

Concerning the “analog” and “derivative”, Applicants have amended the claims to specifically define the structure of such “analog” and “derivative”, thus, this aspect of the rejection is moot.

Moreover, concerning the recitation of “treatment” or “prevention” or “prophylaxis,”

Applicants submit that the claims have been suitably amended. It is further noted that in medicine, the term “prophylaxis” does not mean nor is synonymous to absolute cure or prevention. For instance, Wikipedia includes example of influenza vaccine with 50% reduction of disease ([http://en.wikipedia.org/wiki/Influenza\\_vaccine](http://en.wikipedia.org/wiki/Influenza_vaccine) Vaccination recommendations) and condom as prophylaxis (obviously not 100% prevention).

In <http://www.thefreedictionary.com/prophylactic> the term is defined as prophylactic - preventing or contributing to the prevention of disease; “preventive medicine”; “vaccines are prophylactic”; “a prophylactic drug” preventive, preventative, healthful - conducive to good health of body or mind; “a healthful climate”; “a healthful environment”; “healthful nutrition”; “healthful sleep”; “Dickens's relatively healthful exuberance.”

The U.S. FDA uses the term prophylaxis for partial reduction of disease, see <http://www.medicalnewstoday.com/articles/125299.php>: “Bayer HealthCare LLC announced that the U.S. Food and Drug Administration (FDA) has approved routine prophylaxis with Kogenate(R) FS Antihemophilic Factor (Recombinant) to reduce the frequency of bleeding episodes and the risk of joint damage.” “-- 93 percent of the participants in the routine prophylaxis group showed normal joint function, in contrast to 55 percent in the episodic group,” and US CDC also use the term indicating partial prevention <http://www.cdc.gov/mmwr/PDF/ss/ss5802.pdf>, see page 5, Malaria Infection After Recommended Prophylaxis Use.

These examples indicate the actual meaning of the term for person with ordinary skill in the art and standard use of the term by U.S. medical authorities.

Accordingly, Applicants submit that those of skill in the art are fully able to make and

use the presently claimed subject matter without undue experimentation.

Issue under 35 U.S.C. § 103(a)

Claims 82 and 83 are rejected under 35 U.S.C. § 103(a) as being obvious over Crandall Jr. in view of the definition of chondroitin sulfuric acid and in view of Kodama. Applicants respectfully traverse this rejection.

Applicants submit that the cited art, whether taken alone or in combination, fails to render the present subject matter obvious.

Definition of chondroitinsulphuric acid, Merck index

As a minor notion, chondroitinsulphuric acid is not a standard term and connection with the publication Crandall or content of Crandall if including material of the definition is unambiguous with regard to present invention for several reasons:

1. Examiner refers to an index citing chondroitinsulphuric acid, however the Crandall article refers to chondroitin sulphuric acid, with a space between the terms. As chondroitin and sulphuric acid are also separate terms the meaning is not clear and several other theories could be postulated based on this difference;
2. Crandall is from year 1933 and the references of chondroitinsulphuric acid start from 1944;
3. It is realized that analytics of Crandall is based on uronic acid assay (page 704, line 7 from below) and also dermatan sulphate comprises uronic acid glucuronic acid together with iduronic acid (and GalNAc and sulphate).

On page 2, line 6 the of the Merck index the definition of chondroitinsulphuric acid includes Chondroitin sulphate B which is dermatan sulphate. The IdoA acid of dermatan sulphate makes the molecular non-sulphated backbone structure different from the present invention.

Crandall

A) Substance of Crandall

In case Crandall would disclose chondroitin sulfate with Mw of 50000 this is clearly different from the present invention because present invention describes:

- 1) non sulphated terminal oligosaccharide sequences of the present invention, based on the definitions of the Examiner the material of Crandall is sulphated and thus different. Merck index states for chondroitinsulphuric acid one sulphate per disaccharide unit, see page 1, line 4.
- 2) Terminal structure of Crandall material is not known nor could be unambiguously established, likely there is no way to obtain data from study published 1933. For example, if one assumed that material would have been produced by chondroitin lyase, the terminal uronic acid contains double bond.
- 3) If the material is chondroitin sulfate then it could be much larger polysaccharide than 50 kDa cited by the index. In the case of 50 kDa the polysaccharide would contain over 120 monosaccharide residues while oligosaccharide sequences comprise only less than 10 monosaccharide units. The effect of terminal structure of Crandall in case there could possibly be any similar non-sulphated terminal would disappear due to a low amount of terminal ends.

B) Indication of Crandall

1) Crandall describes large gastric ulcers which are visible from X-rays, this being the terminal form of the disease. The current *H. pylori* indications are associated with earlier phase of diseases before gastric atrophy. In fact it is known that the current *H. pylori* causing gastric ulcers is likely to disappear from atrophic stage of gastritis.

Furthermore, there are numerous other factors causing gastric ulcers such as stress or alcohol, in 1933 in global economy was in major recession and these would have been very prominent. Therefore based on these results, a skilled person would not have considered the ulcers to have been caused by *H. pylori*.

2) Crandall is from the year 1933. Current *H. pylori* infections causing gastric ulcers were discovered 1983 by Warren and Marshall (see Kodama page 2, lines 5-11). It is a scientific fact that infections are emerging diseases caused by sudden mutations [e.g. Spanish Flu, SARS, Swine flu, e.g. see Smith GJD et al Nature 2009 459, 25 June 2009, abstract (enclosed): first sentence “virus (S-01V) emerged” and page 1124 Table 1, with definitive starting time in autumn 2009]. Therefore it cannot be known if *H. pylori* causing gastric ulcers actually existed before 1983, considering a 50 year time difference between 1933 and 1983 likelihood of this is much reduced.

Therefore, any conclusions based on Crandall, without more exact information, would be prevented by multiple reasonable doubts.

Kodama et al.

The substances of Kodama and substances cited on paragraph 8 are very different from Crandall or the present invention:

The patent application describes multiple sulphated polysaccharides, which have totally different backbone structure than chondroitin, including glucose polysaccharides dextran and curdlan, galactose polysaccharides carrageenan and GlcNAc/GlcA/IdoA polysaccharide heparin.

Paragraph 8 refers to polysaccharides of certain bifid bacteria or lactic acid bacteria or seaweed rhamnose materials and discloses that they are useful in prevention or treatment of gastric ulcers. For these material gastric ulcers are without any reference to *H. pylori*, as obvious from above, ulcers can be caused by numerous reasons.

The fucoidan reference is related to *H. pylori*. Fucoidan is a monosaccharide fucose based sulfated polysaccharide.

The Examiner states that paragraph 8 would teach that gastric disorders caused by *H. pylori* are known to be treated with a polysaccharide, but actually only certain different sulphated polysaccharides are mentioned in the whole application.

As it is known for a skilled person and obvious by examining the Tables from present invention that glycan binding by *H. pylori* (or other pathogens) is structure specific phenomenon, there is no possibility to draw any conclusion with regard to *H. pylori* and chondroitin sulphate based on Kodama. Actually, if chondroitin sulphate would have been active in hands of Kodama, one would have assume it claimed with other sulphated polysaccharides with similar price, so Kodama may be teaching away from any *H. pylori* speculation based on Crandall.

The similarities of Kodama and Crandall (without reasonable *H. pylori* association) are not in the chondroitin polysaccharide backbone structures, but presence of polysaccharide and

sulphate, structural features not being the features of present invention. Accordingly, Applicants submit that those of skill in the art would never combine Crandall and Kodama to arrive at the presently claimed subject matter. Therefore, there exists no obviousness.

In view of the above, Applicants request that the Examiner withdraw all rejections and allow the currently pending claims.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Craig A. McRobbie, Reg. No. 42,874, at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

Dated:

JUL 21 2009

Respectfully submitted,

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Attachments: as noted.